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Case Report

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Pregnancy in Primary Ovarian Insufficiency and Hypoplastic Uterus: Case Series

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Abstract

Primary ovarian insufficiency (POI) in women of reproductive age remains unexplained in nearly 90% of cases. Various infections (e.g., mumps, varicella, malaria, shigella, tuberculosis) can destroy healthy ovarian tissue. Rare mutations in genes for FSH and LH receptors, chromosomal abnormalities (e.g., Turner Syndrome, Mosaic Turners, Fragile X FMR1 premutation), and autoimmune diseases (e.g., Addison disease, Hashimoto thyroiditis, rheumatoid arthritis, systemic lupus erythematosus) are also associated with POI. Genetic mutations and autosomal recessive diseases like galactosemia contribute to POI as well.

The overall success rate for pregnancy and live birth after assisted reproductive techniques is only 25%. Women with POI should be informed about their condition and future fertility treatment options.

For women desiring fertility, cyclical bleeding is preferred to maximize chances of successful embryo transfer or natural pregnancy. Premenopausal women are often prescribed OCPs with a placebo week per month, leading to 12 weeks of estrogen deficiency annually. Oocyte donation remains the best option for achieving successful pregnancy in women with POI, with a 40% probability after one IVF cycle and 70-80% after four cycles.

Keywords: POI, IVF, Menstruation, Hypoplastic uterus, Autosomal recessive diseases, Systemic lupus erythematosis, Rheumatoid arthritis, Ovarian tissue

1. Introduction

Primary ovarian insufficiency (POI) in a woman of reproductive age remains unexplained in almost 90% of the cases [1]. There are numerous potential causes of POI such as various infections like mumps, varicella, malaria, shigella, tuberculosis can destroy healthy ovarian tissue, rare mutations in the genes for FSH and LH receptors can alter the ovarian response, chromosomal abnormalities such as Turner Syndrome (45X0) or Mosaic Turners; Fragile X FMR1 premutation substantially decrease the amount of functioning tissue leading to accelerated oocyte depletion early in life [2-4]. Autoimmune diseases such as Addison disease, Hashimoto thyroiditis, rheumatoid arthritis, systemic lupus erythematosis etc. genetic mutations and autosomal recessive diseases such as galactosemia have also been associated with POI [5]. Approximately 4-10% of women with POI may conceive naturally and approximately 20% will have successful ovulation induction. However, the overall success of pregnancy and live birth only reaches 25% after assisted reproductive techniques [6]. Women with such condition should be aware of the condition and need to be explained about the options for future fertility treatment.

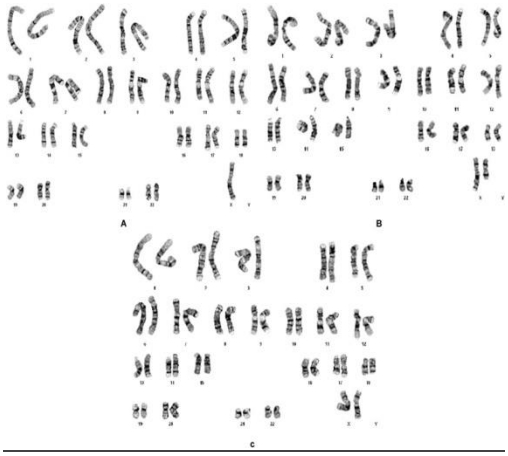
2. Case Reports

2.1 Patient 1

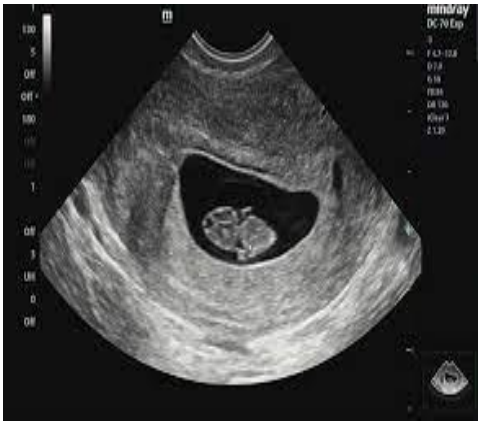
A couple from rural part of West Bengal, India presented with primary infertility for about eighteen months. Both the male and female partners were 21 years of age. The female partner had history of irregular menstrual cycles and had menstruation only with medications. Her height was 136.5 cm and body weight was 41.4 kg. Transabdominal ultrasound (TAS) of the female partner showed hypoplastic uterus (4.5X1.2X1) cm with bilateral streak ovaries. She had no similar history in her other siblings. No genetic disorders were seen in the male partner or other siblings of the female partner. Her Karyotyping was 45XO/46XX–diagnosed as Mosaic Turner's syndrome. Necessary investigations were carried out at our institution. Serum FSH was 73.3 mIU/ml, LH–21.3 mIU/ml, AMH-0.45ng/ml, estradiol level was 48 pg/ml as done on the second day of her menstrual cycle. Transvaginal Ultrasound (TVUS) showed hypoplastic uterus (4.1X1.9X3.2) cm

(Length* Width*Height), with midline endometrium and bilateral streak ovaries. Male Partner's semen analysis showed severe oligoasthenoteratozoospermia. They were offered the option of In-Vitro Fertilization (IVF-ET) with donor sperm and donor oocyte followed by frozen embryo transfer after optimizing the uterine length and vascularity with cyclical oral estrogen and progesterone administration. They had consented for the same. We had started the patient on estradiol valerate tablets twice daily for 21 days and dydrogesterone 10mg tablets twice daily for 10 days every month. Dydrogesterone is a progestin closely related to natural progesterone but it is bioavailable after oral administration and hence the choice [9].

Serial TVUS was done for 3 months to see the outcome of the treatment. Nutritional status of the female partner was optimized before planning of frozen embryo transfer. We continued this treatment for 7 months to achieve an optimum uterine measurement (6.1X3X1.6) cm and vascularity. We planned frozen embryo transfer under down-regulated hormone replacement cycle (DR-HRT cycle). Oral estradiol hemihydrate tablets (2 mg, thrice daily) were started, one month after down regulation with Injection Leuprolide (3.75 mg). TVUS was repeated on tenth day of starting tablet estradiol. Uterine length was (6.1X3.1X1.6) cm with midline triple line endometrium measuring 6.7 mm. 3-D rendition of the uterus revealed no obvious abnormality. Uterus measured (6X3.3X2.2) cm with midline triple line endometrium measuring 8.1 mm with optimum endometrial vascularity (Zone 2). She was started with oil-based progesterone injection from the fourteenth day of starting tablet estradiol. Day-05 blastocyst transfer was done on 6th day of injection progesterone. Two Blastocysts (4AA. 3AB) were transferred under ultrasound guidance by our senior clinician. Serum beta-HCG value was 1500 mIU/ml after 14 days of embryo transfer. TVUS was done on 8 weeks of gestation revealed single live intrauterine gestation with cardiac activity within normal limit. Progesterone and other medications were given as per standard protocol for continuation of pregnancy.



Karyotype report

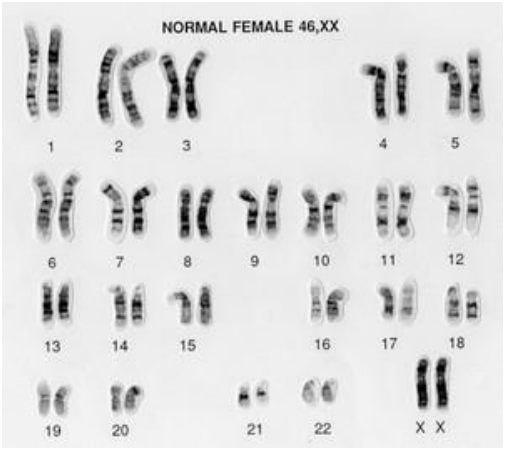


TVUS at 8 weeks gestation period

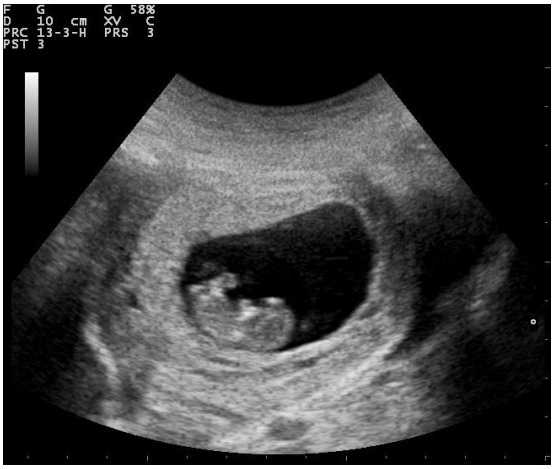
2.2 Patient 2

A couple from West Bengal, India presented with history of primary infertility for about three years, since marriage. The female partner, aged 23 years had history of irregular menstrual cycles and used to have withdrawal bleeding only on consumption of oral contraceptive pills (OCP) which were prescribed by her local doctor. Her height was 151cm and body weight was 57 kg. No genetic disorders were reported in the patient or other siblings of the female partner. Her Karyotyping was normal, 46XX. Necessary investigations were carried out at our institution. Serum FSH was 34 mIU/ml, LH–19 mIU/ml, estradiol level was 17.43 pg/ml as done on the second day of her menstrual cycle. Screening transvaginal Ultrasound (TVUS) showed hypoplastic uterus (4*2.1*2) cm (Length* Width*Height), with midline endometrium and bilateral streak ovaries. Her husband was 32 years old and his semen analysis was normal (WHO). They were offered the option of In-Vitro Fertilization (IVF-ET) with donor oocyte and self-sperm followed by frozen embryo transfer after optimizing the uterine length and vascularity with cyclical oral estrogen and progesterone administration. Similar protocol was followed in HRT. They had consented for the same. Serially, TVUS was done for 4 months to see the outcome of the treatment. We continued this treatment for 6 months to achieve an optimum uterine measurement (6X3X2.5) cm and vascularity. We planned frozen embryo transfer under down-regulated hormone replacement cycle (DR-HRT cycle). Oral estradiol valerate tablets (2 mg, thrice daily) were started, one month after down regulation with Injection Leuprolide (3.75 mg). TVUS was repeated on tenth day of starting tablet estradiol valerate. Uterine length was (6.2X3.2X2) cm with midline triple line endometrium measuring 6.9 mm. 3-D rendition of the uterus revealed no obvious abnormality. Uterus measured (6.2X3.3X2) cm with midline triple line endometrium measuring 8.4 mm with optimum endometrial vascularity (Zone 3). She was started with oil-based progesterone injection from the fourteenth day of starting estradiol tablets. Day-05 blastocyst transfer was done on 6th day of injection progesterone. One blastocysts (4AA) was transferred under ultrasound guidance by our senior clinician. Serum beta-HCG value was 454.35 mIU/ml after 14 days of

embryo transfer. TVUS was done on 7 weeks of gestation revealed single live intrauterine gestation with cardiac activity within normal limit. Progesterone and other medications were continued as per standard protocol.



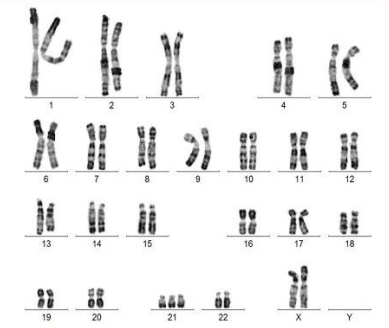
Karyotype report



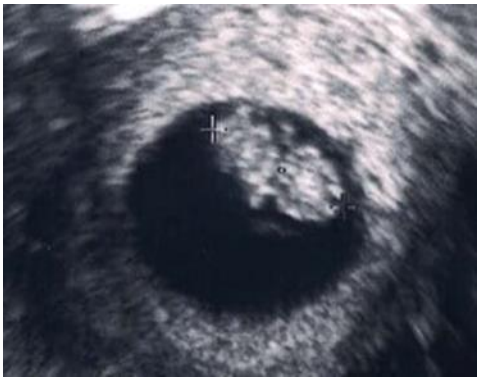
TVUS at 7 weeks gestation period

2.3 Patient 3

Another couple presented to our centre with history of primary infertility for about five years. The female partner, aged 26 years had history of irregular menstrual cycles and used to have menstruation only with medications. Her height was 146cm and body weight was 53 kg. No genetic disorders were reported in the patient or other siblings of the female partner. Her Karyotyping was normal, 46XX. Investigations were carried out at our institution as required. Serum FSH was 32 mIU/ml, LH–20 mIU/ml, Estradiol level was 19.73 pg/ml as done on the second day of her menstrual cycle. Screening transvaginal Ultrasound (TVUS) showed hypoplastic uterus (3.7*2*1.8) cm (Length* Width*Height), with midline endometrium and bilateral streak ovaries. Her husband was 30 years old and his semen analysis was normal (WHO) . They were offered the option of In-Vitro Fertilization (IVF-ET) with donor oocyte and self-sperm followed by frozen embryo transfer after optimizing the uterine length and vascularity with cyclical oral estrogen and progesterone administration, following the same protocol as in the other 2 patients. The couple had consented for the same. TVUS was done serially for 4 months to see the outcome of the treatment. We continued this treatment for 8 months to achieve an optimum uterine measurement (6.15X3X2.5) cm and vascularity. We planned frozen embryo transfer under down-regulated hormone replacement cycle (DR-HRT cycle). Oral estradiol tablets (2 mg, thrice daily) were started, one month after downregulation with Injection Leuprolide (3.75 mg). TVUS was repeated on tenth day of starting tablet estradiol. Uterine length was (6.25X3.3X2) cm with midline triple line endometrium measuring 7.1mm. 3-D rendition of the uterus revealed no obvious uterine abnormality. Uterus measured (6.25X3.3X2.5) cm with midline triple line endometrium measuring 8.8 mm with optimum endometrial vascularity (Zone 2). She was started with oil-based progesterone injection from the fourteenth day of starting tablet estradiol. Day-05 blastocyst transfer was done on 6th day of injection progesterone. Two blastocysts (4AA, 3AA) were transferred under ultrasound guidance by our senior clinician. Serum beta-HCG value was 827.79mIU/ml after 14 days of embryo transfer. TVUS was done on 8 weeks 3 days of gestation revealed single live intrauterine gestation with cardiac activity within normal limit. Progesterone and other medications were continued as per standard protocol.



Karyotype report



TVUS at 8weeks 3 days gestation period

3. Discussion

Women with POI in reproductive age group, who desire fertility, cyclical bleeding is preferred to maximize their chances of successful embryo transfer or even naturally occurring pregnancy [3]. In premenopausal women, usually OCPs are prescribed typically with use of 1 week of placebo per month which sums up to 12 weeks of estrogen deficiency that may result in symptoms associated with a hypoestrogenic state and does not provide adequate physiologic repletion [3,6].

With regard to assisted reproduction and fertility, there is no evidence that ovulation induction can be reliably achieved with gonadotropins or GnRH analogues [6]. Regular supplementation of dehydroepiandrosterone (DHEA) and melatonin in combination with hormone replacement therapy (HRT) have showed a minimal increase in successful pregnancy rates as compared to women on HRT therapy alone, as per a study by Dragojević Dikić S, et al. [7]. The combination of estradiol and dydrogesterone tablets were given in our patients, which did not have any major side-effects [9]. Experimental studies on mice models have attempted ovarian grafts and bone marrow transplants to generate functioning oocytes. But these methods are controversial and clinically inapplicable to the human population [8]. A woman's probability of pregnancy increases to approximately 40% in the setting of oocyte donation after one cycle of IVF and climbs to 70-80% with four cycles of IVF [6]. Oocyte donation is by far considered as the best option for infertility in such women to achieve a successful pregnancy. We have put up these case reports in order to establish and support the fact that in women with POI and hypoplastic uterus assisted reproductive techniques with donor oocytes can act as a miracle and help them to achieve successful pregnancies.

References

1. Sullivan, S. D., Sarrel, P. M., & Nelson, L. M. (2016). Hormone replacement therapy in young women with primary ovarian insufficiency and early menopause. Fertility and sterility, 106(7), 1588–1599.
2. Nelson, L.M. (2009). Clinical practice. Primary ovarian insufficiency. The New England journal of medicine, 360(6), 606–614.
3. Lambrinoudaki, I., Paschou, S. A., Lumsden, M. A., Faubion, S., Makrakis, E., Kalantaridou, S., & Panay, N. (2021). Premature ovarian insufficiency: A toolkit for the primary care physician. Maturitas, 147, 53–63.
4. De Vos, M., Devroey, P., & Fauser, B. C. (2010). Primary ovarian insufficiency. Lancet (London, England), 376(9744), 911–921.
5. Welt C. K. (2008). Primary ovarian insufficiency: a more accurate term for premature ovarian failure. Clinical endocrinology, 68(4), 499–509.
6. Podfigurna-Stopa, A., Czyzyk, A., Grymowicz, M., Smolarczyk, R., Katulski, K., Czajkowski, K., & Meczekalski, B. (2016). Premature ovarian insufficiency: the context of long-term effects. Journal of endocrinological investigation, 39(9), 983–990.
7. Dragojević Dikić, S., Vasiljević, M., Jovanović, A., Dikić, S., Jurišić, A., Srbinović, L., & Vujović, S. (2020). Premature ovarian insufficiency - novel hormonal approaches in optimizing fertility. Gynecological endocrinology : the official journal of the International Society of Gynecological Endocrinology, 36(2), 162–165.
8. Welt C. K. (2008). Primary ovarian insufficiency: a more accurate term for premature ovarian failure. Clinical endocrinology, 68(4), 499–509.
9. Obara-Moszynska, M., Dzialach, L., Rabska-Pietrzak, B., Niedziela, M., & Kapczuk, K. (2021). Uterine Development During Induced Puberty in Girls with Turner Syndrome. Frontiers in endocrinology, 12, 707031.